REMARKS

Claims 1, 2, 5-15, 18-22 and 56-62 are present in the application and stand rejected. As set forth above, Claims 1, 56, 58 and 60-62 have been amended to require that the antibacterial composition additionally contain a pharmaceutically acceptable pH buffering agent for maintaining the pH of the composition in the range of 7.0 to 9.0. Support for this amendment is found in the specification at page 23, line 11. The independent claims have additionally been amended to require that the antibacterial agent be present at a concentration of from 0.04 wt % to 25 wt %. Support for this amendment is found in the specification is found at page 20, line 4. It is believed that Claims 1, 2, 5-15, 18-22 and 56-62 are in condition for allowance in view of the foregoing amendments and following comments. Reconsideration and favorable action is requested.

Rejection of Claims 1, 2, 5-9, 12-15, 19 and 56-62 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1, 2, 5-9, 12-15, 19 and 56-62 under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Mulder (U.S. Patent No. 5,565,189, hereafter the Mulder '189 patent) in view of Raad et al. (U.S. Patent No. 6,267,979, hereafter the Raad '979 patent). The Examiner has cited the Mulder '189 patent as teaching a method of treating infected wounds including applying a composition to the injury comprising a biocide (hydroxyquinoline) and a chelating agent (sodium EDTA) (example 1). The Examiner has indicated that the Mulder '189 patent is silent as to a synergistic relationship between the chelator and the biocide, but indicated that this relationship is well known in the art. The Examiner has cited the Raad '979 patent as disclosing a disinfecting composition comprising a synergistic combination of chelating agents and antimicrobial agents (citing the abstract and example 5). The chelators include various EDTA derivatives along with diethylene triamine pentaacetic acid (DPTA), and triethylene tetramine dihydrochloride (TRIEN) while the antibacterial agents include minocycline, oxytetracycline, tetracycline, gentamicin, and erythromycin (example 5). The EDTA is present in concentrations from 0.1-10,000 ppm (Column 4, lines 35-40). More

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specifically, the Examiner has indicated that in one embodiment of the Raad '979 patent the EDTA is present in a concentration of 30 g/L, which is approximately 102 mM (example 4). It is the position of the Examiner that the concentration of chelators is merely an optimizable limitation as long as synergy is maintained, and in each embodiment of the Raad '797 patent synergy is maintained. Finally, the Examiner has concluded that it would have been obvious to include the synergistic combination of the Raad '979 patent into the method of the Mulder '189 patent in order to improve the biocidal properties of the wound cleanser of prior art.

The Mulder '189 patent discloses a non-sensitizing over-the-counter wound cleanser composed of a carrier portion (70-90 wt% of the cleanser; Column 2, lines 28-35), an emollient portion (up to 10 wt% of the cleanser; Column 2, lines 36-46), a humectant portion (up to 10 wt% of the cleanser; Column 2, lines 47-53), a surfactant portion (up to 10 wt% of the cleanser; Column 2, lines 54-60), a preservative portion (up to 1.5 wt% of the cleanser; Column 2, lines 54-60), and a cosmetic biocide (oxyquinoline, up to 2 wt% of the cleanser; Column 3, lines 3-4).

The carrier portion of the cleanser includes 65-75 wt% of water and 7-13 wt % of aloe vera gel based on the total weight of the cleanser (Column 2, lines 30-32).

The emollient portion is an alkyl stearate, preferably butyl stearate (Column 2, lines 38-42), but may be cetyl, isobutyl, isocetyl, isopropyl, myristal or octyl stearate (Column 2, lines 42-43).

The humectant is glycerine (Column 2, lines 51-53; Table 1, Column 4, line 36).

The surfactant portion is cocamphoacetate (Column 2, lines 57-60; Table 1, Column 4, line 41).

The preservative portion is 0.08-0.12 wt % sodium EDTA or 0.7-1.2 wt % alkyl paraben (Column 2, lines 26, 27, and 63-67; Table 1, Column 4, lines 38 and 39).

The cosmetic biocide portion is hydroxyquinoline, an antiseptic with mild fungistatic, bacteriostatic, anthelmintic, and amebicidal action.

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In addition, the cleanser of the Mulder '189 patent may contain an alkalizer (up to 1% (wt/wt) triethanolamine or sodium borate; Column 4, lines 12-14) or an acid/conjugate base buffering system, to maintain the pH of the cleanser within the range of 6.5 to 6.8; vitamin E (up to 1 wt% of the cleanser; Column 3, lines 16-18) to assist in reepithelialization of a wound site; and cocamide DEA (up to 5 wt% of the cleanser; Column 3, lines 19-22) to act as a viscosifier.

The Raad '979 patent discloses a method for controlling biofouling in water treatment, pulp and paper manufacture, and oil field water flooding applications with a combination of an antifungal or antibiotic and a chelator (see Field of the Invention, Column 1, lines 12-17). As stated in the Raad '979 patent at Columns 8 and 9:

> The present invention provides compositions and methods for the prevention and treatment of biofouling in water containing or submerged systems. The invention arises from the inventors' discovery that chelators have a significant growth inhibitory effect against species of fungal and bacterial microorganisms including Aspergillus, Fusarium, Candida, Pseudomonas, vancomycin-resistant enterococci, and multidrug resistant Stenotrophomonas (see data in FIG. 1, FIG. 2, FIG. 3, FIG. 4, FIG. 12, FIG. 13 and FIG. 14). Also, the inventors have demonstrated that, when combined with antifungal agents, chelators show additive to synergistic inhibitory activity against the growth of fungal microorganisms (see data in FIG. 5, FIG. 6, FIG. 7, FIG. 8, FIG. 9, FIG. 10 and FIG. 11). The inventors have further demonstrated that, when combined with antimicrobial compounds, chelators show additive to synergistic inhibitory activity against the growth of bacterial microorganisms (see data in FIG. 15, FIG. 16 and FIG. 17). These discoveries provide the basis for a novel program of prevention and treatment of microbial biofoulings using any of several embodiments of the inventive formulations, which may comprise various combinations of chelators, antifungal agents, antiseptic agents, antibacterial agents, and any necessary buffers, solvents, or surfactants.
>
> All pipelines, including those which carry gas, oil, and water or other chemicals become contaminated with bacterial and fungal microorganisms. The same is true for commercial and industrial aqueous process and water handling systems. These microorganisms form biofilm on the surfaces of these pipelines and systems. This biofilm or slime comprises the glycocalyx of the microbial organisms contained therein. Most eukaryotic cells have a carbohydrate-rich zone about their periphery, and this peripheral zone or cell coat is made up of oligosaccharide side chains of glycolipids and integral membrane glycoproteins. Embedded in the biofilm environment, microorganisms such as bacteria and fungi benefit from a

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> form of "extrinsic" resistance, thus rendering organisms which are ordinarily intrinsically and biologically sensitive to antimicrobials more resistant than they would otherwise be.
>
> Colonies that include several kinds of bacteria and fungi can form deposits on metal surfaces, building slime layers and producing organic acids that cause pitting and accelerate corrosion of pipelines and associated metal structures. The inventors have shown that EDTA and other chelators of the present invention assist in disrupting and/or dissolving the glycocalyx of microbial colonies adherent to venous catheters. See, for example, U.S. Pat. No. 5,362,754 by Raad et al., or U.S. patent application Ser. No. 08/317,309 by Raad et al., both of which are herein incorporated by reference. The disruption and/or dissolution of microbial slime improves the activity of antimicrobial compounds against the bacteria, fungi, and other microbes embedded in the slime.

As is readily apparent from the foregoing, the field of the Raad '979 patent is totally unrelated to the field of invention of the present application and the Mulder '189 patent. Accordingly, there is no basis for any person of ordinary skill in the art to look to the field of microbial biofouling in gas, oil, and water applications to modify the teachings of the Mulder '189 patent.

In addition, there is no basis in the generic disclosure of the Raad '979 patent for arriving at the methods of applicants' amended claims. With respect to chelating agents, the Raad '979 patent discloses at Column 4, lines 35-49:

> The chelators of the present invention may be delivered to an aqueous system at a dosage ranging from about 0.1 parts per million (ppm) to about 10,000 ppm, more preferably at a dosage ranging from about 1.0 ppm to about 5000 ppm, and most preferably at a dosage ranging from about 50 ppm to about 2500 ppm, including all intermediate dosages therebetween. It will be readily understood that "intermediate dosages", in these contexts, means any dosages between the quoted ranges, such as about 0.1. 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, etc.; 3, 4, 5, 6, 7, 8, 9, 10, etc.; 12, 13, 14, etc.; 50, 51, 52, 53, 54, etc.; 100, 101, 102, 103, 104, etc.; 500, 501, 502, 503, etc.; 600, 700, 800, 900, 1000, etc.; 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, and about 10,000 ppm, and including all fractional dosages therebetween.

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With respect to antibiotic agents, the Raad '979 patent discloses at Column 6, lines 45-59:

> The antibiotics of the present invention may be delivered to an aqueous system at a dosage ranging from about 0.01 parts per million (ppm) to about 1000 ppm, more preferably at a dosage ranging from about 0.1 ppm to about 100 ppm, and most preferably at a dosage ranging from about 0.5 ppm to about 10 ppm, including all intermediate dosages therebetween. It will be readily understood that "intermediate dosages", in these contexts, means any dosages between the quoted ranges, such as about 0.01, 0.02, 0.03, etc.; 0.1. 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, etc.; 3, 4, 5, 6, 7, 8, 9, 10, etc.; 12, 13, 14, etc.; 50, 51, 52, 53, 54, etc.; 100, 101, 102, 103, 104, etc.; 500, 501, 502, 503, etc.; 600, 700, 800, 900, and about 1000 ppm, and including all fractional dosages therebetween.

In addition to the foregoing, the Raad '979 patent is silent as to pH levels required to obtain synergistic activity.

As set forth above, the independent claims of the application have been amended to require that the antibacterial compositions contain from 0.04 wt % to 25 wt % of the antibacterial agent, that the chelating agent is present in the composition at a concentration in the range of 0.1 mM to 100.0 mM, and that the composition contain a pharmaceutically acceptable pH buffering agent for maintaining the pH of the composition in the range of 7.0 to 9.0. Accordingly, even if there were some motivation for a person skilled in the art to modify the cosmetic formulation of the Mulder '189 patent with the industrial anti-sliming components of the Raad '979 patent (with which applicants disagree), there is no basis for selecting from the extremely broad generic description of the Raad '979 patent the synergistic amounts of antibacterial agent and chelating agent of applicants' claims. In addition, even if combined the resulting modified formulation of the Mulder '189 patent would have a pH outside of the range required by applicants' amended claims.

In view of the foregoing amendments and comments, it is respectfully submitted that Claims 1, 2, 5-9, 12-15, 19, and 56-62 would not have been obvious under 35 U.S.C. 103(a) over the combined disclosures of the Mulder '189 patent in view of the Raad '979 patent, and that this rejection of claims should properly be withdrawn.

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Rejection of Claims 1 and 18-22 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1 and 18-22 under 35 U.S.C. § 103(a) as being unpatentable over the combined disclosures of the Mulder '189 patent and the Raad et al. '979 patent, as discussed above, in view of Cuny et al. (U.S. Patent No. 6,207,679 hereafter the Cuny '679 patent). Claims 18-22 are directed to the method of Claim 1 wherein the skin injury is a burn, an abrasion, an ulcer or a lesion of the oral mucosa, or the composition is a mouthwash, respectively. It is the Examiner's position that specific injuries would be obvious to treat to the artisan of ordinary skill since the general problem of eliminating a bacterial infection at a wound site is disclosed in the prior art. According to the Examiner, specific injuries are well within the level of skill in the art prior art as seen in the Cuny '679 patent.

As discussed in applicants' response filed January 29, 2007, the Cuny et al. '679 patent is directed to new antibacterial compounds--a specifically disclosed family of 2-(3-indolyl)-4-quinolinocarboxamide compounds and their substituted derivatives. Although the Cuny et al. '679 patent contains a generic disclosure of virtually all pharmaceutically acceptable routes of administration of the compounds and does indicate that wetting agents, emulsifiers and lubricants, coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants (including EDTA) can also be present in compositions of the new family of compounds, there is no disclosure or remote suggestion of topically administering a composition synergistic concentrations of a pharmaceutically acceptable antibacterial agent and a pharmaceutically acceptable chelating agent selected from EDTA, TRIEN and diethyltriamin-pentaacetic acid (DPTA), together with tris (hydroxymethyl) aminomethane (TRIZMA Base), and a pharmaceutically acceptable carrier, as required by applicants' amended claims. Accordingly, the Cuny et al. '679 patent does not overcome the deficiencies of the Mulder '189 patent and the Raad '979 patent, as discussed in detail above.

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 1 and 18-22 would not have been obvious under 35 U.S.C. § 103(a) over the combined

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disclosures of the Mulder '189 patent and the Raad et al. '979 patent in view of the Cuny '679 patent, and that this rejection should properly be withdrawn.

Rejection of Claims 10 and 11 Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 10 and 11 under 35 U.S.C. 103(a) as being unpatentable over the Mulder '189 patent and the Raad '979 patent in view of Kruse et al. (U.S. Patent No. 5,646,151 hereafter the Kruse '151). Claims 10 and 11 relate to the method of Claim 1 wherein the pharmaceutically acceptable antibacterial agent is amikacin or neomycin, respectively.

As set forth above, the Mulder '189 patent and the Raad '979 patent have been improperly combined by the Examiner and, even if combined, fail to disclose or suggest applicants' claimed invention. The Kruse et al. '151 patent does not disclose or suggest either synergistic combinations of antibacterial agents and chelating agents, or the specific compositions of applicants' claimed invention, and does nothing to overcome the basic deficiencies of the Mulder '189 patent and the Raad '979 patent. Applicants' Claims 10 and 11 would not have been obvious to any person of ordinary skill in the art within the meaning of 35 U.S.C. § 103(a) over this combination of references. It is believed that the Examiner's rejection of Claims 10 and 11 should properly be withdrawn.

Provisional Obviousness-Type Double Patenting

The Examiner has provisionally rejected Claims 1, 2, 5-11, and 56-62 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 12-15, 18-21, 25-29, 43 and 44 of copending Application No. 10/739,841. Since both Application No. 10/739,841 and the current application are subject to rejection(s) on other grounds, this rejection will be addressed when nonstatutory obviousness-type double patenting is the only rejection remaining pursuant to MPEP § 804.

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CONCLUSION

In view of the foregoing claim amendments and arguments, applicants respectfully submit that Claims 1, 2, 5-15, 18-22, and 56-62 are in condition for allowance. Reconsideration and favorable action are requested. The Examiner is further requested to contact applicants' representative at the number set forth below to discuss any issues that may facilitate prosecution of this application.

Respectfully submitted,

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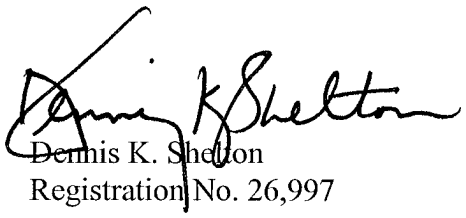

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